Mechanical and Thermal Damage Accumulation and Recovery in Cell and Tissue Products

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2nd Sept 2008

Background:

The successful delivery of cell/tissue based products from factory to bedside is one of the key challenges for commercialisation of regenerative medicine. Cell/tissue based products will experience mechanical and thermal impacts to some extent during transportation. Although plenty of research has been carried out to identify the biological response of cell/tissue to mechanical stress and hypothermic/hyperthermic exposure, most of this research is in a physiological or pathological context.

Mechanical impact:

It is known that cells within a skeleton system sense and correspond to the mechanics they experience [1]. However, little is know about the extent of mechanical impact experienced by cell/tissue–based products and the threshold that would induce accumulative non-reversible damage during transportation. Information gathered from in vitro research on the effects of cumulative mechanical force to cells and tissues[2,3] would be a good lead for using mathematical modelling techniques to understand the underlining biophysics.

Thermal impact:

Most of the researchers in the field of cryobiology believe that the mechanism of damage caused during freezing with low cooling rates is chemical and related to the hypertonicity of the extracellular solution. However, there is some evidence to indicate that cells may be destroyed during freezing also by compression between ice crystals. It has been demonstrated experimentally, and also by mathematical modelling, that cell viability decreases steeply when cells are compressed to 30% of their original diameter[4].

Problem statement:

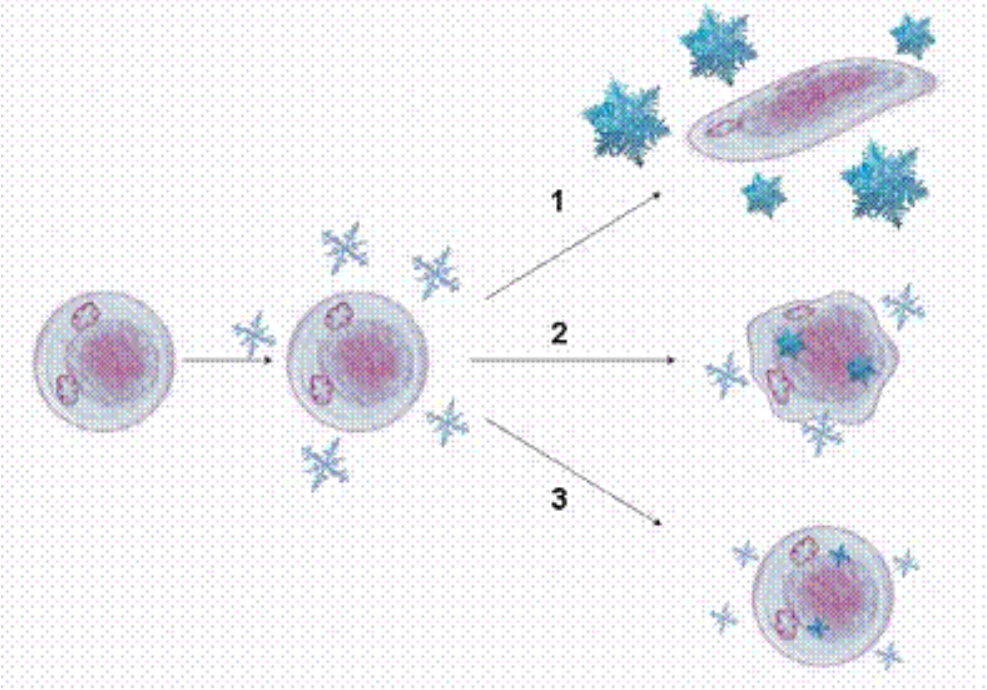
Typically, there are two types of delivery state of cell/tissue based products, frozen or growing.

1. **Frozen products**: How does the rate of temperature change affect the
    a) phase change of water,
    b) cell size,
    c) dehydration and re-hydration of cell body,
    d) local electrolyse concentration
    e) osmosis cross cell membrane

and what would be the cumulative effect of these changes?

2. **Growing products**: What is the influence of
   a) air,
   b) space above,
   c) temperature change of shipping environment,
   d) shear force,
   e) gas-liquid interface

to the growing cells or tissue containing growing cells?



Cooling rate and intracellular and extracellular crystal formation
1. Slow cooling 2. Fast Cooling 3. Very fast Cooling

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